UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VYTACERA BIO, LLC, Plaintiff, v. CYTOMX THERAPEUTICS, INC., Defendant.	Case No. Jury Trial Demanded

COMPLAINT FOR PATENT INFRINGEMENT

Vytacera Bio, LLC ("Vytacera" or "Plaintiff") by and through its counsel, files this Complaint against CytomX Therapeutics, Inc. ("CytomX" or "Defendant") for infringement of United States patent nos. 8,809,504 ("the '504 patent") and 9,775,913 ("the '913 patent) (collectively the "patents-in-suit"), and alleges as follows:

NATURE OF THE ACTION

1. This is an action for infringement of the patents-in-suit arising under the patent laws of the United States, 35 U.S.C. §§ 100, *et seq.* Specifically, this action relates to patents covering molecules inhibiting biologically active compounds and further comprising moieties specifically cleavable by a reagent produced by a target cell.

PARTIES

2. Plaintiff Vytacera Bio, LLC ("Vytacera"), is a Delaware corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 140 Ramona Road, Portola Valley, California 94028.

3. On information and belief, Defendant CytomX Therapeutics, Inc., ("CytomX"), is a corporation organized under the laws of Delaware, with its principal

place of business at 151 Oyster Point Boulevard, Suite 400, South San Francisco, California 94080. On information and belief, Defendant CytomX Therapeutics, Inc. uses, manufactures, imports, sells, or offers to sell the Probody™ technology platform, in an effort to conduct basic research and identify and develop pharmaceutical compounds for distribution throughout the United States, including this judicial district.

SUBJECT MATTER JURISDICTION AND VENUE

4. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a) because this is a patent infringement action that arises under the patents laws of the United States, 35 U.S.C. §§ 100 *et seq*.

5. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391(b), (c), (d) and/or 1400(b).

PERSONAL JURISDICTION OVER DEFENDANTS

6. Plaintiff incorporates each of the preceding paragraphs as if fully set forth here.

7. This Court has personal jurisdiction over Defendant by virtue of, *inter alia*, its presence in Delaware, its systematic and continuous contacts with Delaware, and the conduct of business with other Delaware corporations.

8. On information and belief, Cogency Global Inc., 850 New Burton Road, Suite 201, Dover, Delaware, is CytomX's registered agent in Delaware and is authorized to accept service on CytomX's behalf.

9. This Court also has personal jurisdiction over Defendant, in part, because Defendant is a registered Delaware corporation. Thus, Defendant has purposefully availed itself of the privileges of conducting business in Delaware.

BACKGROUND

Dr. Lauermann's Groundbreaking Research Leading to the Patents-in-Suit

10. Plaintiff incorporates each of the preceding paragraphs as if fully set forth here.

11. Vit Lauermann, Ph.D. is an accomplished microbiologist and geneticist.

12. Dr. Lauermann received his Ph. D. in microbiology and genetics from the Charles University located in Prague, Czech Republic. Founded in 1348, Charles University is one of the most prestigious universities in Eastern Europe.

13. Following the receipt of his degree, Dr. Lauermann was a Postdoctoral Fellow at Johns Hopkins University in Baltimore, Maryland, and later, a Senior Research Fellow at the National Cancer Institute.

14. During his accomplished career, Dr. Lauermann has written numerous research papers published in a litany of well-regarded academic journals.

15. Dr. Lauermann also holds multiple patents covering various aspects of his life-long research.

16. As part of his research, Dr. Lauermann developed novel, groundbreaking platform technology directed to the treatment of various disease states, with patents filed as early as 2002.

17. This groundbreaking research included the development of platform technology that assists with the delivery of biologics compounds to specific cells, while limiting the side effects of the compounds.

18. In particular, the platform technology includes inhibitors suppressing the biological activity of administered agents, which might have undesirable systemic effects, until they are in the proximity of targeted cells. At the targeted cells, the inhibitors are inactivated or cleaved from the agents by an enzyme or reagent secreted by target cells. This specific release of the inhibitors increases the active agent's activity and concentrations at a disease site allowing the active agent to reach concentration levels that have desired therapeutic effects only at the targeted cells.

19. This groundbreaking research and the methods for its application are covered in Dr. Lauermann's patents, which are discussed below.

United States Patent No. 8,809,504

20. U.S. Patent No. 8,809,504, entitled "Inhibitor which is deactivatable by a reagent produced by a target cell" (attached as Exhibit 1), was duly and legally issued on August 19, 2014.

21. The '504 patent claims priority to September 3, 2002.

22. The inventor named on the '504 patent is Vit Lauermann.

23. The '504 patent will expire on or about July 24, 2028.

24. The claims of the '504 patent are valid, enforceable, and not expired.

25. Vytacera owns all rights, title and interests in the '504 patent.

26. CytomX does not have a license to practice the inventions claimed in the '504 patent.

United States Patent No. 9,775,913

27. U.S. Patent No. 9,775,913, entitled "Method of site-specific activation of an antibody by a protease" (attached as Exhibit 2), was duly and legally issued on October 3, 2017.

28. The '913 patent claims priority to September 3, 2002.

29. Vit Lauermann is the inventor of the '913 patent.

30. The '913 patent will expire on or about August 30, 2023.

31. The claims of the '913 patent are valid, enforceable, and not expired.

32. Vytacera owns all rights, title and interests in the '913 patent.

33. CytomX does not have a license to practice the inventions claimed in the '913 patent.

CytomX Therapeutics, Inc.'s Infringing Acts

34. On information and belief, CytomX Therapeutics, Inc. (later converted from an LLC to an Inc.) was founded in 2008 by Frederick Gluck, Dr. Nancy Stagliano, and Professor Patrick Daugherty of UC Santa Barbara's Department of Chemical Engineering, to combat the lack of selectivity by drug candidates.

35. On information and belief, CytomX engages in the business of offering to sell or selling drug discovery services and products to pharmaceutical company customers in the United States and abroad.

36. On information and belief, the drug discovery services and products CytomX has sold to its United States-based pharmaceutical company customers were developed through making and using the infringing Probody™ platform technology and associated methods.

37. As used herein, "Probody™ technology platform," includes the inhibitors, recognition domains, antibodies and methods, which involve selective activation in the targeted microenvironment while reducing peripheral drug activity, developed by CytomX.

38. On information and belief, CytomX started as an emerging medical technology company applying molecular engineering and microfluidic cell separation technologies to develop protein therapeutics and integrated medical diagnostic devices.

39. On information and belief, a license from UC Santa Barbara specifically grants CytomX "an exclusive or non-exclusive license in the Field under the Licensed Patent Rights as set forth in Exhibit B to make, have made, use, sell, offer for sale and import Licensed Products and Licensed Services and to practice Licensed Method to the extent permitted by law."[1]

40. Through technology licensed from UC Santa Barbara, CytomX developed its Probody™ technology platform and associated methods, allowing for drug designs that selectively activate in the tumor microenvironment while reducing drug activity in

[1] *See* https://www.sec.gov/Archives/edgar/data/0001501989/000119312515322694/d948537dex1021.htm.

healthy tissue and in circulation. In fact, CytomX has spent over ten years conducting research to characterize protease activity and to engineer proteins to take advantage of specific proteases. In addition, CytomX devised criteria for identifying proteases that would work best in the context of its Probody™ technology platform.[2] Thus, the inhibitors, recognition domains, antibodies and methods claimed in the patents-in-suit, which involve selective activation in the tumor microenvironment while reducing drug activity in healthy tissue, are used by CytomX as a research tool to identify targets and/or to screen inhibitors.

41. CytomX further sells and offers for sale the Probody™ technology platform in the United States and abroad to pharmaceutical companies.

42. CytomX's business has been built around exploiting the Probody™ technology platform that Vytacera pioneered and patented, and selling and offering it for sale to pharmaceutical companies, the platform that Vytacera pioneered and patented.

43. On information and belief, CytomX makes (and/or has made for its behalf) and uses the Probody™ technology platform as a part of research activities that are unrelated to a particular pharmaceutical compound, particular biological process, and/or a particular physiological effect.

44. On information and belief, CytomX has sold and continues to sell data and research services from the Probody™ technology platform that were developed in

[2] *See e.g.* http://ir.cytomx.com/static-files/3103fd17-30cd-4d0c-882d-418fdf6830c9.

part from research activities that are unrelated to a particular pharmaceutical compound, particular biological process, and/or a particular physiological effect.

45. On information and belief, CytomX makes and uses the Probody™ technology platform, including compounds, as part of the Probody™ technology platform's commercialization, preparation, and manufacturing related activities that are unrelated to a particular pharmaceutical compound, particular biological process, and/or a particular physiological effect.

46. On information and belief, at least some of CytomX's sales are memorialized in commercial agreements with its pharmaceutical company customers, pursuant to which CytomX agreed to transfer property and/or perform services for a certain price. On information and belief, these agreements typically involve CytomX performing some combination of the following activities in exchange for cash consideration: (1) assays using the Probody™ technology platform for the discovery and/or identification of possible protein targets, (2) validation experiments from the Probody™ technology platform designed to determine whether inhibition of a target protein is therapeutically relevant, (3) synthesis and testing of a number of Probody™ technology platform's inhibitors (typically hundreds or thousands) to screen for effectiveness, and (4) transfer of Probody™ technology platform's associated methods, research data from the Probody™ technology platform, and information concerning potential targets from the Probody™ technology platform to pharmaceutical company customers for further validation and development. These commercial sales or offers for sale are infringements of the patents-in-suit in the United States.

47. On information and belief, in return for the sale of the compounds, inhibitors and methods claimed in the patents-in-suit, CytomX received substantial payments from pharmaceutical companies.

48. Upon information and belief, revenues from CytomX's Probody™ technology platform are generated through different avenues:

> The Company's [CytomX's] revenues are primarily derived through its license, research, development and commercialization agreements. The terms of these types of agreements may include (i) licenses for the Company's technology or programs, (ii) research and development services, and (iii) services or obligations in connection with participation in research or steering committees. Payments to the Company under these arrangements typically include one or more of the following: nonrefundable upfront and license fees, research funding, milestone and other contingent payments to the Company for the achievement of defined collaboration objectives and certain preclinical, clinical, regulatory and sales-based events, as well as royalties on sales of any commercialized products.

See 2019 Annual Report at 101.[3]

49. In sum, on information and belief, CytomX has engaged in an enterprise of offering for sale and selling to its pharmaceutical company customers, drug discovery services and drug candidates that infringe the patents-in-suit.

50. 35 U.S.C. § 271(e)(1) ("Section 271(e)(1)") defines a safe harbor against patent infringement:

> It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

[3] *See* http://ir.cytomx.com/static-files/c5dc3917-7bf9-4a95-a918-53cd4381c598

51. This provision entered title 35 in 1984 as part of the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (the "1984 Act"). The House Committee that initiated this provision characterized its limits, noting that the "nature of the interference with the rights of the patent holder" would not be substantial," but "*de minimus* [sic]." H.R. Rep. No. 857, reprinted in 1984 U.S.C.C.A.N. at 2692, 2714 (stating that "all that the generic can do is test the drug for purposes of submitting data to the FDA for approval. Thus, the nature of the interference is *de minimus* [sic].").

52. In 2005, the Supreme Court reaffirmed that not all drug discovery and research under the 1984 Act was subject to the Section 271(e)(1) clinical trial exemption, holding that the exemption may exist where "a drug-maker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is 'reasonably-related' to the 'development and submission of information under . . . federal law.'" *Merck KGaA v. Integra Lifesciences I, Ltd*., 545 U.S. 193, 207 (2005) (quoting the text of Section 271(e)(1)); s*ee also, Amgen Inc. v. Hospira, Inc.,* 336 F.Supp.3d 333 (D.Del. 2018) *aff'd*, 944 F.3d 1327 (Fed. Cir. 2019).

53. The Federal Circuit has held that research tools used in drug discovery and development, and are not themselves the subject of regulatory approval, fall outside the protection of Section 271(e)(1). *Proveris Scientific Corp. v. Innovasystems, Inc*., 536 F.3d 1256, 1265 (Fed. Cir. 2008).

54. On information and belief, CytomX's offering to sell and sale of its Probody™ technology platform and drug discovery services and products led to collaborations with pharmaceutical companies and research institutions, including, but not limited to, Bristol-Meyers Squibb Company, AbbVie Ireland Unlimited Company, Pfizer Inc., ImmunoGen, Inc., Amgen Inc. and, MD Anderson, to identify and develop potential inhibitor targets using the Probody™ technology platform. These pharmaceutical companies made upfront payments to CytomX in order to fund, without limitation, basic research and development to identify potential target molecules, and to identify and develop specific inhibitors for these target molecules.[4]

55. On information and belief, and as described in CytomX's Annual Reports, CytomX booked over one hundred million dollars of revenue from sales of Vytacera's patented technology.[5] On information and belief, CytomX's sales are in whole or in part not reasonably related to the development and submission of information to the FDA for regulatory approval, and therefore are not exempted from infringement by the safe harbor provision of 35 U.S.C. § 271(e)(1). Rather, on information and belief, the substantial sums that CytomX has received, and the significant future payments contemplated by the CytomX-pharmaceutical company agreements, relate in whole or in part to CytomX's business activities that fall outside of the safe harbor provision of 35 U.S.C. § 271(e)(1).

[4] *See e.g.* http://ir.cytomx.com/static-files/3103fd17-30cd-4d0c-882d-418fdf6830c9.
[5] *See* http://ir.cytomx.com/financial-information/annual-reports; and http://ir.cytomx.com/static-files/c5dc3917-7bf9-4a95-a918-53cd4381c598.

56. According to CytomX's Annual Reports, CytomX shows recognized revenue of $57.5 million in 2019; $59.5 million in 2018; $71.6 million in 2017; $12.8 million in 2016; and 5.9 million in 2015.[6] CytomX's revenues are generated in part from CytomX's collaboration and other commercial activities.

57. On information and belief, CytomX entered into two agreements with Bristol-Meyers Squibb Company and has received $250 million in upfront payments, development service fees of $10.8 million, $12 million in milestone payments and additional research funding up to $3,586 million from Bristol-Meyers Squibb Company.[7]

58. On information and belief, CytomX entered into an agreement with AbbVie Ireland Unlimited Company, received $10 million in upfront payments and additional research funding to discover new targets, and is eligible for an additional $275 million in payments. [8]

59. On information and belief, CytomX entered into an agreement with Pfizer Inc., received $25 million in upfront payments, and additional research funding up to $610 million.[9]

60. On information and belief, CytomX entered into an agreement with ImmunoGen, Inc. CytomX gave limited access to its Probody™ database to

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[6] *Id.*
[7] *See e.g.* http://ir.cytomx.com/financial-information/annual-reports; http://ir.cytomx.com/static-files/c5dc3917-7bf9-4a95-a918-53cd4381c598; and http://ir.cytomx.com/node/9521/pdf.
[8] *Id.*
[9] *Id.*

ImmunoGen, Inc. in exchange for $60 million in upfront payments, as well as gaining limited access to ImmunoGen, Inc.'s drug conjugate technology, from which CytomX obtained exclusive worldwide development and commercial rights to ImmunoGen's preclinical epithelial cell adhesion molecule (EpCAM)-targeting program that was developed utilizing CytomX's Probody™ platform technology and ImmunoGen's drug conjugate technology, which is of significant value.[10]

61. On information and belief, CytomX entered into an agreement with Amgen Inc. CytomX received $40 million in upfront payments, stock purchases of $20 million and additional research funding from Amgen Inc.[11]

62. On information and belief, CytomX also entered into a research and collaboration agreement with MD Anderson.[12] The financial terms of these agreements were not disclosed.[13]

63. On information and belief, through the licensing arrangement with UC Santa Barbara, CytomX was required to make significant license payments to UC Santa Barbara of more than $10 million for the use of UC Santa Barbara's patented technology.[14]

64. On information and belief, CytomX's use of Vytacera's patented technology is directed toward creating its own patented inventions, as evidenced by

[10] *Id.*
[11] *Id.*
[12] *Id.*
[13] *Id.*
[14] *Id.*

CytomX's issued and pending patent applications. On information and belief, the research performed by CytomX in support of its patent applications, was wholly or partially unrelated to the development and submission of any information to the FDA.

65. On information and belief, CytomX's pharmaceutical industry customers are responsible for development and regulatory approval of drug products. Regardless of whether the pharmaceutical company customers later identify and develop some of the resulting inhibitors and eventually advance an inhibitor to a phase of development where the Section 271(e)(1) exemption may apply, CytomX's commercial transactions, and the activities related to such transactions, are wholly or partially unrelated to the generation of data for submission to the FDA.

66. In addition to completed sales and past offers for sale, on information and belief, CytomX continues to sell and offer for sale in the United States the products and methods claimed in the patents-in-suit. On information and belief, CytomX is actively pursuing transactions with potential customers where it will transfer inhibitors and/or perform the methods claimed in the patents-in-suit for a stated price. These activities undermine the value of the patents-in-suit and the technology that the patents protect.

67. On information and belief, the publicly known agreements between CytomX and its pharmaceutical company customers represent profitable sales by CytomX of technology and materials that infringe the patents-in-suit. Further, CytomX's commercial agreements amount to offers for sale in the United States that depress and harm the value of Vytacera's patents, as detailed here. CytomX has built a commercial enterprise that depends on the sale, offer for sale, use and importation of

Vytacera's patented technology. CytomX's acts of infringement, as further detailed here, are inflicting harm on Vytacera, *inter alia*, in the form of lost or value-diminished licensing opportunities.

CytomX Therapeutics, Inc.'s Willful Infringement

68. On information and belief as early as 2014, Dr. Lauermann contacted CytomX with an offer to license the '504 patent and the patent application that led to the issuance of the '913 patent.

69. Dr. Lauermann provided CytomX with a copy of the '504 patent, and indicated that another related patent was going to issue, i.e. the '913 patent. He also provided a detailed claim analysis showing that the '504 patent covered CytomX's activities. Dr. Lauermann also offered his significant technical expertise to CytomX.

70. Dr. Lauermann and his representatives spent months attempting to negotiate with CytomX. But after these discussions, CytomX refused to continue negotiations, thereby rejecting Dr. Lauermann's licensing overtures.

71. On information and belief, CytomX prevented Dr. Lauermann from offering a license to other pharmaceutical companies.

72. On information and belief, CytomX makes, uses, and sells its Probody™ technology platform with full knowledge that its Probody™ technology platform related activities infringed and infringe the patents-in-suit.

73. On information and belief, CytomX has full knowledge of its infringement of the patents-in-suit and continues to use the Probody™ technology platform with reckless disregard for Plaintiff's patent rights.

PATENT INFRINGEMENT

Count I - Infringement of United States Patent No. 8,809,504

74. The allegations set forth above are re-alleged and incorporated by reference as if they were set forth fully here.

75. Defendant makes, uses, offers to sell, and/or sells the Probody™ technology platform, within the United States, and/or imports into the United States the Probody™ technology platform that infringes (literally and/or under the doctrine of equivalents) at least claims 1-2, 4, 6-9, 11, 13, 15-17 of the '504 patent

76. Defendant's Probody™ technology platform infringes the '504 patent.[15]

77. By way of example, claim 1 of the '504 patent covers:

> An inhibitor which is deactivatable by a reagent produced by a target cell comprising:
>
> > (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of a biologically active agent wherein said first moiety is operably linked to;
> >
> > (b) a second moiety specifically cleavable by a protease produced by a target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding activity of said inhibitor.

78. Claim 2 of the '504 patent further covers:

> The inhibitor of claim 1, wherein said first moiety is selected from the group consisting of a peptide, a cyclic peptide, or a polypeptide.

79. Claim 4 of the '504 patent further covers:

[15] *See* https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf.

The inhibitor of claim 1, wherein said inhibitor is selected from the group consisting of an antibody inhibitor, or a dimer or multimer of the above.

80. Claim 6 of the ’504 patent further covers:

The inhibitor of claim 1 wherein at least one said second moiety is operably linked to the first moiety.

81. Claim 7 of the ’504 patent further covers:

The inhibitor of claim 1 wherein said first and second moieties are connected by a peptide, or a chemical linker.

82. Claim 8 of the ’504 patent further covers:

The inhibitor of claim 1, wherein said second moiety is selected from the group consisting of a peptide, a polypeptide, or a conjugate of the above.

83. Claim 9 of the ’504 patent further covers:

The inhibitor of claim 1 wherein said second moiety is a peptide which comprises a sequence cleavable by a protease.

84. Claim 11 of the ’504 patent further covers:

The inhibitor of claim 1 wherein said reagent is selected from the group consisting of a protease.

85. Claim 13 of the ’504 patent further covers:

The inhibitor of claim 1 wherein said reagent is produced by activated or proliferating endothelial cells, tumor cells, or leukemia cells.

86. Claim 15 of the ’504 patent further covers:

The inhibitor of claim 1 which further comprises or associates with a recognition domain that binds to a target structure, an exterior surface of a targeted cell, a cell surface marker, an extracellular matrix, or components thereof.

87. Claim 16 of the ’504 patent further covers:

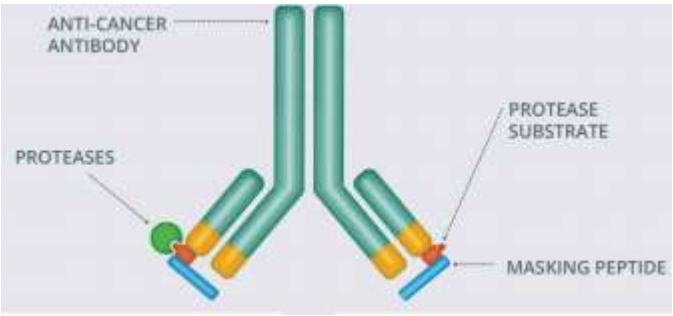
The inhibitor of claim 15, wherein said recognition domain binds to activated or proliferating endothelial cells, to tumor cells, or to leukemia cells.

88. Claim 17 of the '504 patent further covers:

> The inhibitor of claim 15, wherein said recognition domain is selected from the group consisting of an antibody, a monoclonal antibody, a bispecific antibody, an antibody fragment, a single chain antibody, a peptabody, or compositions and variants thereof.

89. CytomX's Probody™ technology platform meets each and every element of claims 1-2 of the '504 patent.

90. CytomX makes, uses, sells, offers to sell and/or imports the Probody™ technology platform, comprising inhibitors that are deactivatable by reagents produced by target cells.[16]

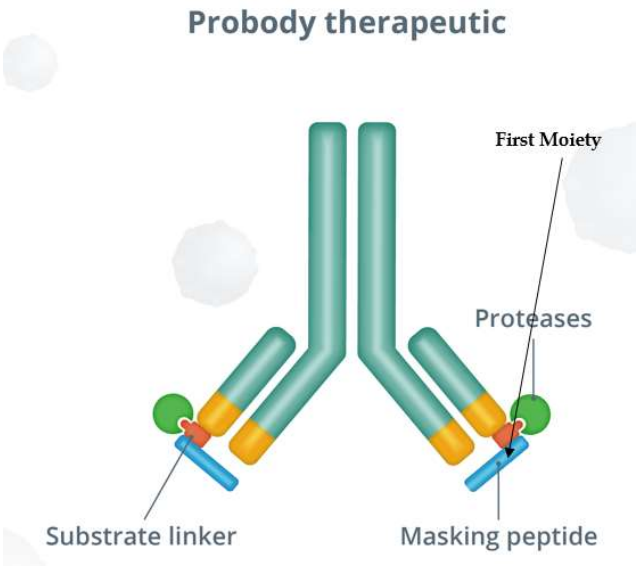


https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf

91. CytomX's Probody™ technology platform comprises inhibitors that contain a first moiety that is a masking peptide that binds, inhibits, suppresses, neutralizes, or decreases the activity of anti-cancer antibody, which acts as a biologically

[16] CytomX has developed a number of inhibitors with its Probody™ platform technology, including without limitation, CX-072, CX-2009, BMS-986249, CX-2029, BMS-986288, EGFR-TCB inhibitors and EpCAM-PDC inhibitors. The Probody™ technology platform is representative of the inhibitors that CytomX has developed and is developing.

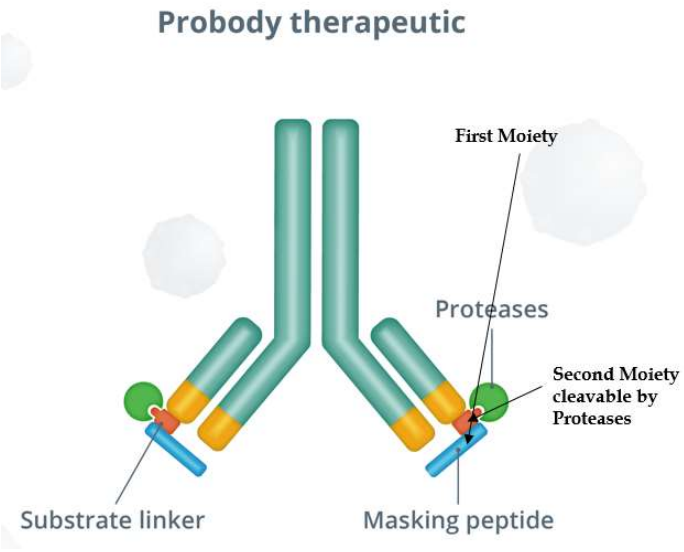
active agent. The masking peptides of the Probody™ technology platform's inhibitors are operably linked to a second moiety.[17]



92. CytomX's Probody™ technology platform's inhibitors contain a second moiety that is cleavable by a protease produced by the target cell. [18]

[17] *See* https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf; https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work.

[18] *See* https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf; https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work.



93. On information and belief, the first and second moieties of CytomX's Probody™ technology platform's inhibitors are not attached in nature.

94. As shown in the figures below, the specific cleavage of the second moiety of CytomX's Probody™ technology platform's inhibitors cause reduction of binding activity of said inhibitor.

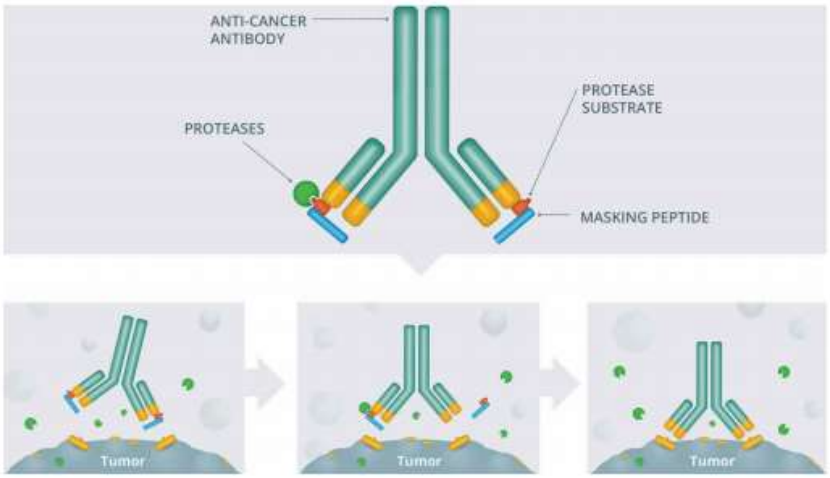


Figure 1. Design of a Probody therapeutic – a protease-activatable, masked antibody prodrug.

The mask (blue) may be a peptide, protein or other moiety that is either expressed as a recombinant extension of the antibody chain(s) (green) or is conjugated such that it blocks access of the cognate antigen to the antigen binding site of the antibody (yellow). The mask is attached to the antibody via a protease cleavable linker (red). Upon entering the tumor microenvironment (lower left), proteases cleave the linker (center), the mask falls away and the antibody binds to the tumor antigen (lower right).

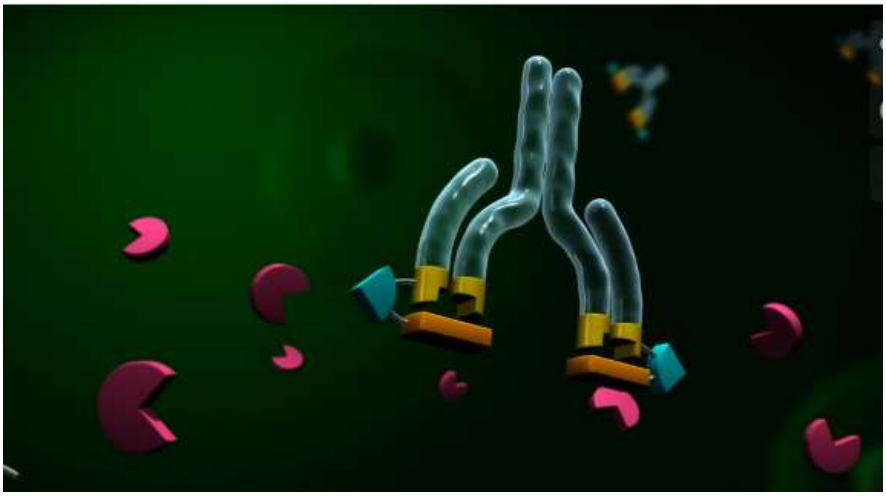
https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf

95. As such, CytomX's Probody™ technology platform meets each and every element of claims 1 and 2 of the '504 patent.

96. CytomX's Probody™ technology platform's inhibitors consist of an antibody inhibitor.

97. As such, CytomX's Probody™ technology platform meets each and every element of claim 4 of the '504 patent.

98. CytomX's Probody™ technology platform's inhibitors comprise a first and second moiety connected by a peptide.



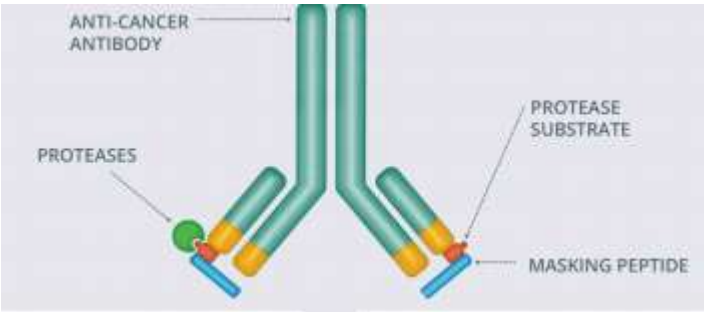
https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work

99. As such, CytomX's Probody™ technology platform meets each and every element of claims 6-7 of the '504 patent.

100. On information and belief, CytomX's Probody™ technology platform's inhibitors comprise a second moiety that are peptides.

101. As such, CytomX's Probody™ technology platform meets each and every element of claim 8 of the '504 patent.

102. CytomX's Probody™ technology platform's inhibitors comprise a second moiety that are peptides that are cleavable by proteases.



https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf

https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work

103. As such, CytomX's Probody™ technology platform meets each and every element of claim 9 of the '504 patent.

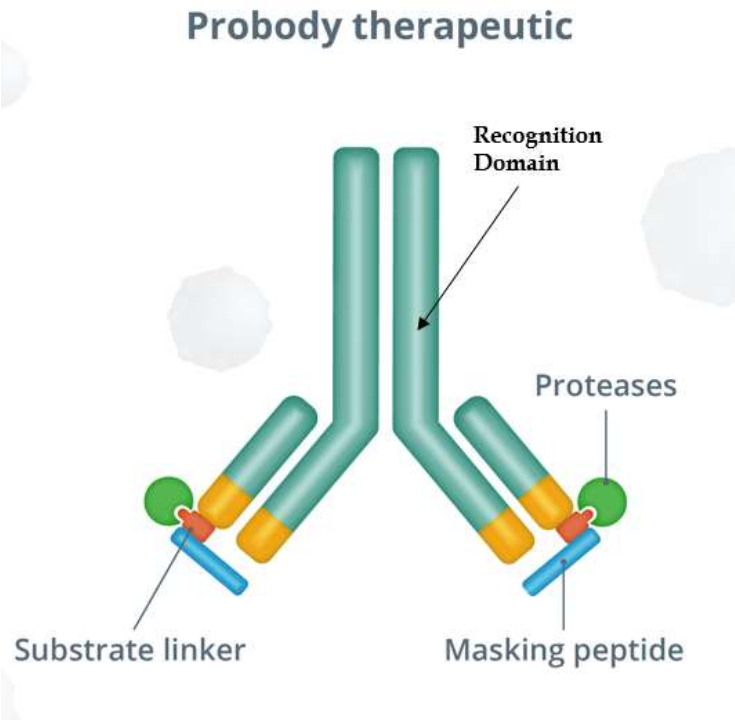
104. CytomX's Probody™ technology platform's inhibitors comprise reagents that are proteases.

105. As such, CytomX's Probody™ technology platform meets each and every element of claim 11 of the '504 patent.

106. CytomX's Probody™ technology platform's inhibitors are deactivatable by protease reagents produced by tumor cells.

107. As such, CytomX's Probody™ technology platform meets each and every element of claim 13 of the '504 patent.

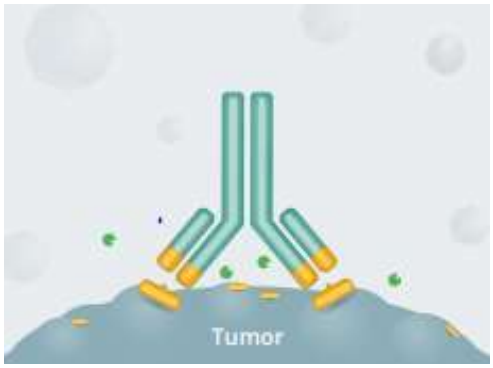
108. CytomX's Probody™ technology platform's inhibitors comprise or associate with recognition domains that bind to target structures, exterior surfaces of targeted cells, cell surface markers, extracellular matrices, or components thereof.



https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work

109. As such, CytomX's Probody™ technology platform meets each and every element of claim 15 of the '504 patent.

110. CytomX's Probody™ technology platform's inhibitors comprise or associate with recognition domains that bind to activated or proliferating endothelial cells, to tumor cells, or to leukemia cells.



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111. As such, CytomX's Probody™ technology platform meets each and every element of claim 16 of the '504 patent.

112. CytomX's Probody™ technology platform's inhibitors comprise or associate with recognition domains that are selected from the group consisting of an antibody, a monoclonal antibody, a bispecific antibody, an antibody fragment, a single chain antibody, a peptabody, or compositions and variants thereof.

113. As such, CytomX's Probody™ technology platform meets each and every element of claim 17 of the '504 patent.

114. On information and belief, Defendant has been on notice of its infringement of the '504 patent since at least as early as 2014, the year in which Dr. Lauermann disclosed the patent and his inventions to Defendant.

115. On information and belief, CytomX's Probody™ technology platform directly infringes at least claims 1-2, 4, 6-9, 11, 13, 15-17 of the '504 patent through their making, using, selling, and/or offering to sell CytomX's Probody™ technology platform.

116. Plaintiff reserves the right to assert additional claims of the '504 patent that CytomX infringes.

117. CytomX's direct infringement of the '504 patent has damaged Plaintiff, and Plaintiff is suffering and will continue to suffer irreparable harm and damages as a result of this infringement.

118. CytomX is, therefore, liable to Plaintiff in an amount that adequately compensates Plaintiff for CytomX's infringement, which, by law, cannot be less than a reasonable royalty, together with interest and costs as fixed by this Court under 35 U.S.C. § 284.

119. On information and belief, CytomX has willfully infringed the '504 patent. Plaintiff is entitled to increased damages of three times the damages assessed pursuant to 35 U.S.C. § 284, as well as an award of attorney's fees pursuant to 35 U.S.C. § 285.

Count II- Infringement of United States Patent No. 9,775,913

120. The allegations set forth above are re-alleged and incorporated by reference as if they were set forth fully here.

121. CytomX makes, uses, offers to sell, and/or sells the Probody™ technology platform, within the United States, and/or imports into the United States CytomX's Probody™ technology platform, and/or by actively inducing infringement by others under § 271(b) and/or contributing to infringement under § 271(c), that infringes

(literally and/or under the doctrine of equivalents) at least claims 1-10, 12-22 of the '913 patent.

122. CytomX's Probody™ technology platform infringe the '913 patent.

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123. By way of example, claim 1 of the '913 patent covers:

> A method of site specific activation of an antibody comprising administration of an inhibitor which is deactivatable by a protease produced by a target cell comprising:
>
> (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of said antibody wherein said first moiety is operably linked to
>
> (b) a second moiety comprising a polypeptide specifically cleavable by said protease produced by said target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding, inhibiting, suppressing, or neutralizing activity of said inhibitor and restoration of activity of said antibody; said inhibitor is administered alone or together with said antibody such that the activity of said antibody is reduced until it reaches said target cell producing said protease wherein the inhibitor is cleaved by said protease and activity of said antibody is restored.

124. Claim 2 of the '913 patent further covers:

> The method of claim 1, wherein said first moiety comprises a polypeptide.

125. Claim 3 of the '913 patent further covers:

> The method of claim 2, wherein the polypeptide is selected from the group consisting of a peptide, and a cyclic peptide.

126. Claim 4 of the '913 patent further covers:

> The method of claim 1, wherein said first moiety comprises a polypeptide that binds, inhibits, suppresses, neutralizes, or decreases activity of a monoclonal antibody, a bispecific antibody, and a single chain antibody.

127. Claim 5 of the ’913 patent further covers:

The method of claim 1, wherein said inhibitor is selected from the group consisting of a monoclonal antibody inhibitor, a bispecific antibody inhibitor, and a single chain antibody inhibitor or a combination thereof.

128. Claim 6 of the ’913 patent further covers:

The method of claim 1, wherein said antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody and a single chain antibody or a combination thereof.

129. Claim 7 of the ’913 patent further covers:

The method of claim 1, wherein said first and second moieties are connected by a peptide or a chemical linker.

130. Claim 8 of the ’913 patent further covers:

The method of claim 1, wherein said first and said second moieties are connected by a peptide comprising a polyglycine serine linker.

131. Claim 9 of the ’913 patent further covers:

The method of claim 1, wherein said second moiety is a polypeptide which comprises a sequence cleavable by two or more proteases.

132. Claim 10 of the ’913 patent further covers:

The method of claim 1, wherein said second moiety is a polypeptide which comprises a sequence cleavable by a serine or cysteine protease.

133. Claim 12 of the ’913 patent further covers:

The method of claim 1, wherein said protease comprises a cysteine protease.

134. Claim 13 of the ’913 patent further covers:

The method of claim 1, wherein said protease comprises a serine protease.

135. Claim 14 of the ’913 patent further covers:

The method of claim 1, wherein said protease is selected from the group consisting of a prostate specific antigen, a matrix metalloproteinase, a plasminogen activator, a urokinase, a urokinase-type plasminogen activator, a tissue-type plasminogen activator, and a matriptase or a combination thereof.

136. Claim 15 of the '913 patent further covers:

The method of claim 1, wherein said protease is produced by a proliferating endothelial cell, a tumor cell, and a leukemia cell.

137. Claim 16 of the '913 patent further covers:

The method of claim 1, wherein said inhibitor further comprises a recognition domain that binds to an exterior surface of the targeted cell, or an extracellular matrix.

138. Claim 17 of the '913 patent further covers:

The method of claim 16, wherein said recognition domain binds to a proliferating endothelial cell, a tumor cell, and a leukemia cell.

139. Claim 18 of the '913 patent further covers:

The method of claim 16, wherein said recognition domain comprises an antibody.

140. Claim 19 of the '913 patent further covers:

The method of claim 16, wherein said recognition domain is selected from the group consisting of a monoclonal antibody, a bispecific antibody, and a single chain antibody or a combination thereof.

141. Claim 20 of the '913 patent further covers:

The method of claim 1, wherein said target cell comprises a tumor cell.

142. Claim 21 of the '913 patent further covers:

The method of claim 1, wherein said administration to a vertebrate results in a desired site specific activation of said antibody.

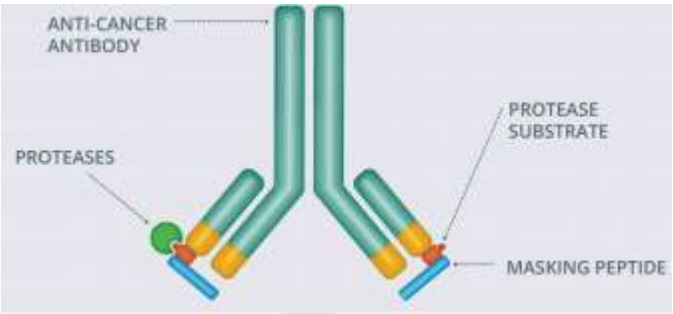
143. Claim 22 of the '913 patent further covers:

> A method of site specific activation of a monoclonal antibody, a bispecific antibody and a single chain antibody or a combination thereof comprising administration of an inhibitor which is deactivatable by a reagent produced by a target cell comprising:
>
> > (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof wherein said first moiety is operably linked to
> >
> > (b) a second moiety comprising a polypeptide specifically cleavable by said reagent comprising a protease produced by said target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding, inhibiting, suppressing, or neutralizing activity of said inhibitor and restoration of activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof; said inhibitor is administered alone or together with said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof such that the activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof is reduced until it reaches said target cell producing said reagent wherein the inhibitor is cleaved by said reagent and activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof is restored.

144. CytomX's Probody™ technology platform meets each and every element of claims 1 and 22 of the '913 patent.

145. CytomX makes, uses, sells, offers to sell and/or imports the Probody™ technology platform. CytomX's Probody™ technology platform uses methods, itself and on behalf of others, for antibodies where there are site specific activations of antibodies comprising administration of inhibitors that are deactivatable by proteases produced by target cells.[19]

[19] CytomX has developed a number of inhibitors with its Probody™ platform technology, including without limitation, CX-072, CX-2009, BMS-986249, CX-2029, BMS-



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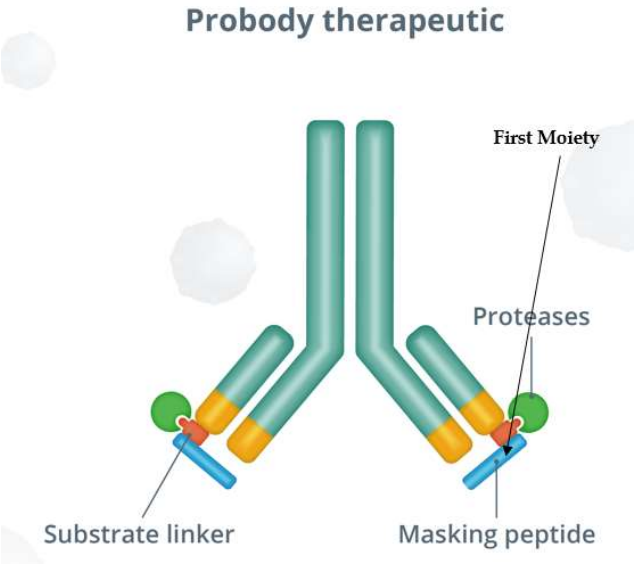
146. CytomX's Probody™ technology platform's inhibitors contain first moieties that neutralize the activity of the antibodies.



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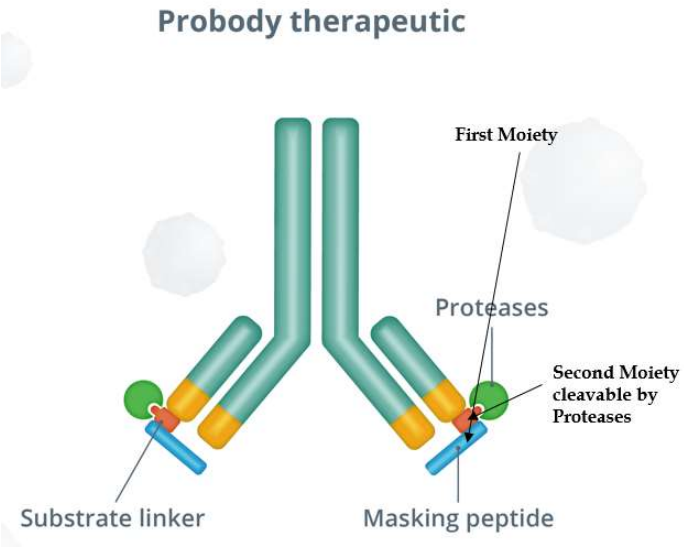
986288, EGFR-TCB inhibitors and EpCAM-PDC inhibitors. The Probody™ technology platform is representative of the inhibitors that CytomX has developed and is developing.

147. CytomX's Probody™ technology platform's inhibitors contain second moieties that are cleavable by proteases produced by the target cells.



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https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work

148. The first and second moieties of CytomX's Probody™ technology platform's inhibitors are not normally attached in nature. The specific cleavage of the second moieties cause reduction of binding activity of the CytomX's Probody™ technology platform's inhibitor.

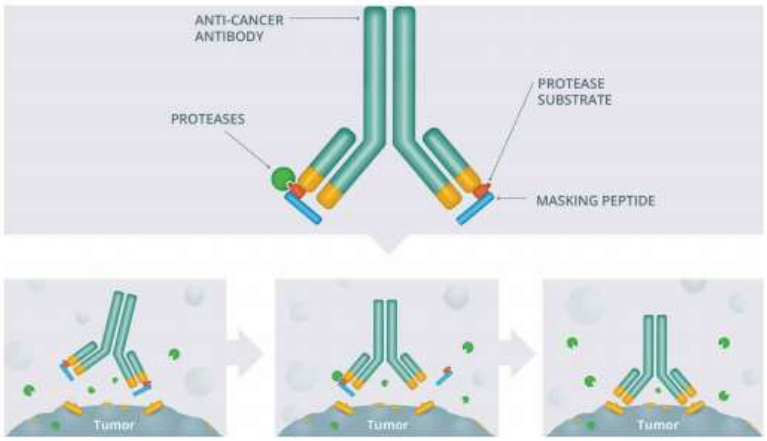
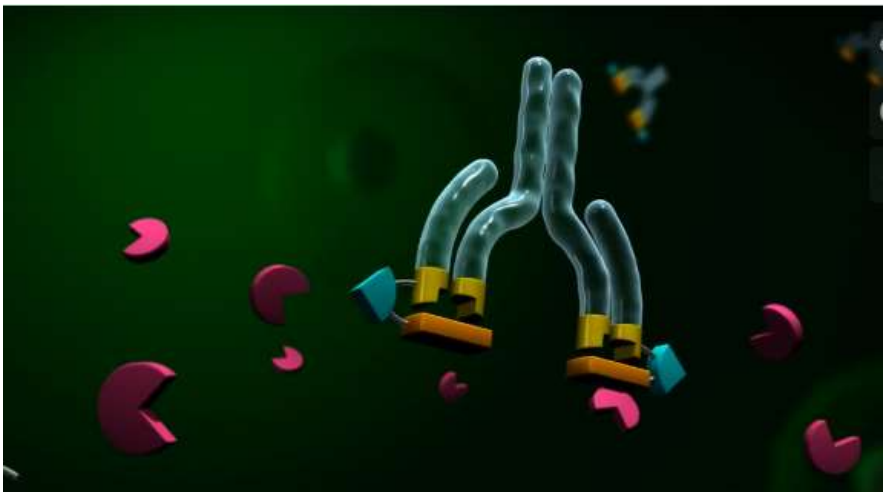


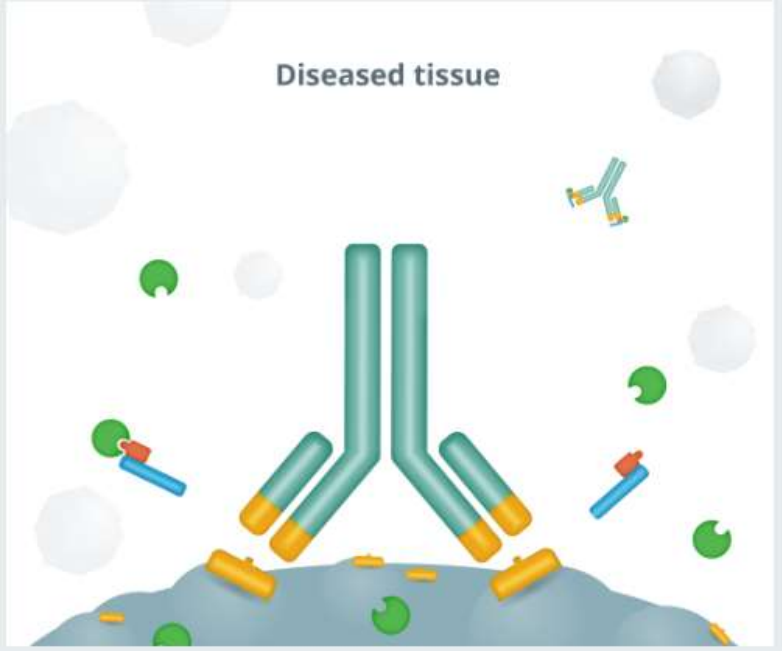
Figure 1. Design of a Probody therapeutic – a protease-activatable, masked antibody prodrug.

The mask (blue) may be a peptide, protein or other moiety that is either expressed as a recombinant extension of the antibody chain(s) (green) or is conjugated such that it blocks access of the cognate antigen to the antigen binding site of the antibody (yellow). The mask is attached to the antibody via a protease cleavable linker (red). Upon entering the tumor microenvironment (lower left), proteases cleave the linker (center), the mask falls away and the antibody binds to the tumor antigen (lower right).

https://cytomx.com/wp-content/uploads/Antibody-Prodrugs-in-Cancer-Review.pdf

149. The activity of CytomX's Probody™ technology platform's antibodies are reduced until they reach the target cells, then after cleavage of the CytomX's Probody™ technology platform's inhibitors the activity of the antibodies are restored.





In the tumor environment, protease enzymes are expected to cleave the substrate, removing the "mask" and activating the Probody therapeutic to bind to its target on cancer cells.

https://cytomx.com/probody-therapeutics/#how-probody-therapeutics-work

150. As such, CytomX's Probody™ technology platform meets each and every element of claims 1 and 22 of the '913 patent.

151. The first moieties of CytomX's Probody™ technology platform's inhibitors are peptides.

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152. As such, CytomX's Probody™ technology platform meets each and every element of claims 2 and 3 of the '913 patent.

153. The first moiety of CytomX's Probody™ technology platform's inhibitors comprise peptides that are capable of binding, inhibiting, suppressing, neutralizing, or

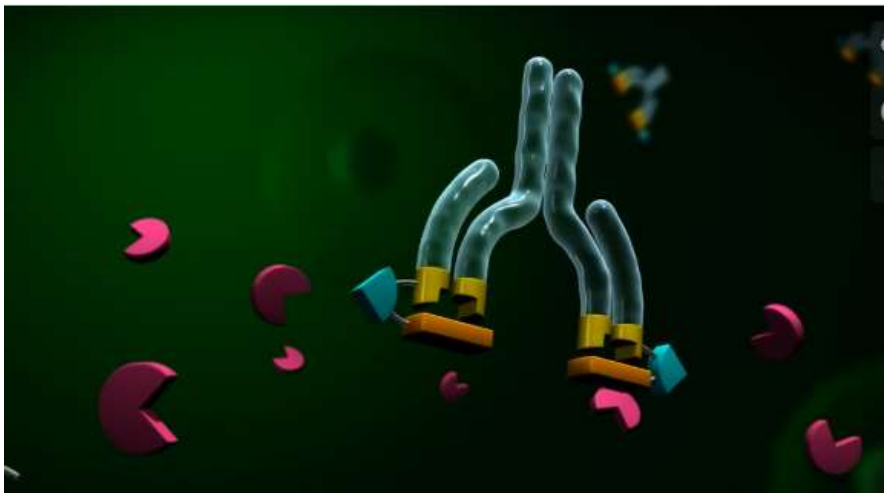
decreasing activity of monoclonal antibodies, bispecific antibodies, and/or single chain antibodies.

154. As such, CytomX's Probody™ technology platform meets each and every element of claim 4 of the '913 patent.

155. Upon information and belief, CytomX's Probody™ technology platform's inhibitors consist of monoclonal antibody inhibitors, bispecific antibody inhibitors, and/or single chain antibody inhibitors or combinations thereof.

156. As such, CytomX's Probody™ technology platform meets each and every element of claims 5 and 6 of the '913 patent.

157. On information and belief, the first and said second moieties of CytomX's Probody™ technology platform's inhibitors are connected by peptides comprising polyglycine serine linkers.



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158. As such, CytomX's Probody™ technology platform meets each and every element of claims 7 and 8 of the '913 patent.

159. Upon information and belief, the second moiety of CytomX's Probody™ technology platform's inhibitors are polypeptides which comprise sequences cleavable by two or more proteases.

160. As such, CytomX's Probody™ technology platform meets each and every element of claim 9 of the '913 patent.

161. Upon information and belief, the second moiety of CytomX's Probody™ technology platform's inhibitors are polypeptides which comprise sequences cleavable by serine or cysteine proteases.

162. As such, CytomX's Probody™ technology platform meets each and every element of claim 10 of the '913 patent.

163. Upon information and belief, the proteases of CytomX's Probody™ technology platform's inhibitors comprise cysteine proteases.

164. As such, CytomX's Probody™ technology platform meets each and every element of claim 12 of the '913 patent.

165. Upon information and belief, the proteases of CytomX's Probody™ technology platform's inhibitors comprise serine proteases.

166. As such, CytomX's Probody™ technology platform meets each and every element of claim 13 of the '913 patent.

167. Upon information and belief, the proteases of CytomX's Probody™ technology platform's inhibitors are selected from prostate specific antigens, matrix metalloproteinases, plasminogen activators, urokinases, urokinase-type plasminogen

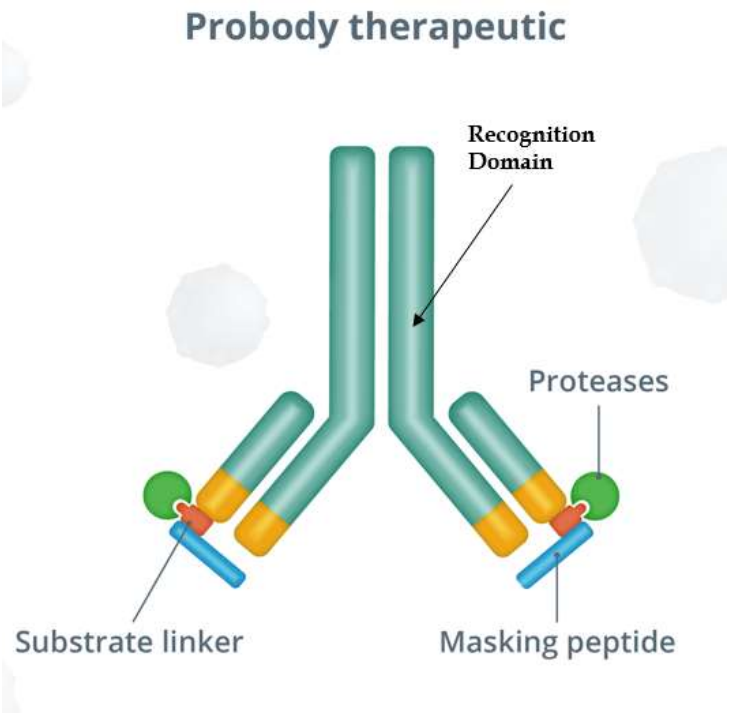
activators, tissue-type plasminogen activators, and/or matriptases or a combination thereof.

168. As such, CytomX's Probody™ technology platform meets each and every element of claim 14 of the '913 patent.

169. Upon information and belief, the proteases of CytomX's ProbodyTM technology platform are produced by a proliferating endothelial cell, a tumor cell, and a leukemia cell.

170. As such, CytomX's Probody™ technology platform meets each and every element of claim 15 of the '913 patent.

171. CytomX's Probody™ technology platform contains recognition domains that bind to exterior surfaces of the targeted cells, or extracellular matrices.



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172. As such, CytomX's Probody™ technology platform meets each and every element of claim 16 of the '913 patent.

173. Upon information and belief, the recognition domains of CytomX's Probody™ technology platform bind to proliferating endothelial cells, tumor cells, and/or leukemia cells.

174. As such, CytomX's Probody™ technology platform meets each and every element of claim 17 of the '913 patent.

175. Upon information and belief, the recognition domains of CytomX's Probody™ technology platform comprise antibodies and monoclonal antibodies.

176. As such, CytomX's Probody™ technology platform meets each and every element of claims 18 and 19 of the '913 patent.

177. Upon information and belief, the target cells of CytomX's Probody™ technology platform are tumor cells.

178. As such, CytomX's Probody™ technology platform meets each and every element of claim 20 of the '913 patent.

179. On information and belief, administration of CytomX's Probody™ technology platform's inhibitors to vertebrates results in desired site specific activation of said antibodies.

180. As such, CytomX's Probody™ technology platform meets each and every element of claim 21 of the '913 patent.

181. On information and belief, CytomX has been on notice of the application that led to the '913 patent since at least as early as 2014, the year that Dr. Lauermann disclosed the patent application and invention to Defendant.

182. On information and belief, CytomX directly infringes at least claims 1-10, and 12-22 of the '913 patent through its use of methods claimed in the '913 patent to develop CytomX's Probody™ technology platform in the United States, which they are making, using, selling, offering to sell and/or importing.

183. On information and belief, CytomX knows that the use of its Probody™ technology platform induces infringement of the '913 patent.

184. CytomX, acting without authority, consent, right, or license of the '913 patent, has induced, and continues to induce partners and collaborators to administer and use the Probody™ technology platform in a manner that directly infringes one or more claims of the '913 patent under 35 U.S.C. § 271(b). More specifically, CytomX's partners and collaborators directly infringe (literally and/or under the doctrine of equivalents) at least claims 1-10, 12-20, and 22 of the '913 patent by using the Probody™ technology platform, resulting in conduct that constitutes, at a minimum, patent infringement under 35 U.S.C. § 271(a).

185. CytomX possessed, and continues to possess, specific intent to induce infringement by providing to its partners and collaborators, at a minimum, the Probody™ technology platform, which provides instructions on how to use the Probody™ technology platform in a manner that infringes directly the '913 patent.

186. As such, CytomX has actively induced and encouraged, and continues to actively induce and encourage, partners and collaborators to use the Probody™ technology platform, resulting in conduct that constitutes, at a minimum, patent infringement under 35 U.S.C. § 271(b).

187. Upon information and belief, CytomX knows that the Probody™ technology platform and its use are especially made or adapted for uses that infringe the '913 patent, that the Probody™ technology platform is not a staple article or commodity of commerce, and that the Probody™ technology platform and its methods are not suitable for substantial non-infringing use, resulting in conduct that constitutes, at a minimum, patent infringement under 35 U.S.C. § 271(c). More specifically, partners and collaborators directly infringe (literally and/or under the doctrine of equivalents) at least claims 1-10, and 12-22 of the '913 patent by using the Probody™ technology platform, resulting in conduct that constitutes, at a minimum, patent infringement under 35 U.S.C. § 271(a).

188. CytomX's foregoing actions constitute and/or will constitute infringement of the '913 patent, active inducement of infringement of the '913 patent, and contribution to the infringement by others of the '913 patent.

189. Upon information and belief, CytomX has acted with full knowledge of the '913 patent and without a reasonable basis for believing that it would not be liable for infringement of the '913 patent, active inducement of infringement of the '913 patent, and/or contribution to the infringement by others of the '913 patent.

190. Plaintiff reserves the right to assert additional claims of the '913 patent that CytomX infringes, either directly or indirectly.

191. CytomX's direct and indirect infringement of the '913 patent has damaged Plaintiff, and Plaintiff is suffering and will continue to suffer irreparable harm and damages as a result of this infringement.

192. CytomX is, therefore, liable to Plaintiff in an amount that adequately compensates Plaintiff for CytomX's infringement, which, by law, cannot be less than a reasonable royalty, together with interest and costs as fixed by this Court under 35 U.S.C. § 284.

193. On information and belief, CytomX has willfully infringed the '913 patent. Plaintiff is entitled to increased damages of three times the damages assessed pursuant to 35 U.S.C. § 284, as well as an award of attorney's fees pursuant to 35 U.S.C. § 285.

JURY DEMANDED

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Plaintiff requests a trial by jury on all issues so triable.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully requests the Court to enter judgment in its favor and against Defendant as follows:

a. finding that CytomX has infringed one or more claims of the '504 and '913 patents;

b. awarding Plaintiff damages under 35 U.S.C. § 284, or otherwise permitted by law, including treble damages based on Defendant's willful infringement, and damages for any continued post-verdict infringement;

c. awarding Plaintiff pre-judgment and post-judgment interest on the damages award and costs;

d. declaring this case exceptional pursuant to 35 U.S.C. § 285;

e. awarding costs of this action and attorney's fees pursuant to 35 U.S.C. § 285, or as otherwise permitted by the law; and

f. awarding such other costs and further relief the Court determines to be just and equitable.

Dated: March 4, 2020

Respectfully submitted,

STAMOULIS & WEINBLATT LLC

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